

endogenously in the cell, and selected from the group consisting of a heterologous expression control sequence and an amplification gene,

(ii) a sequence encoding a positive selection marker,

(iii) at least two target sequences for a site-specific recombinase flanking the sequences of (i) and (ii), and

(iv) DNA sequences which flank the sequences of (i), (ii) and (iii) and are homologous to a nucleic acid section in the genome of the cell in order to allow a homologous recombination,

(b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place,

(c) isolating the cell obtained according to step (b), and

(d) expressing the at least one sequence of (i) to thereby change the expression of the nucleic acid sequence which is present endogenously in the cell.

23. The process as claimed in claim 20, further comprising, after step (d), cutting the sequences of (i) and (ii) flanked by the site-specific recombinase target sequences out of the genome of the cell by transient activation of a site-specific recombinase that recognizes the target sequences.

24. A vector suitable for homologous recombination, comprising the following sequences

(i) at least one sequence selected from the group consisting of an expression control sequence and an amplification gene each of which upon expression is capable of changing the expression of the nucleic acid sequence which is present endogenously in the cell,

(ii) a sequence encoding a positive selection marker,

(iii) at least two target sequences for a site-specific recombinase flanking the sequences of (i) and (ii), and

(iv) DNA sequences which flank the sequences of (i), (ii) and (iii) and are homologous to a nucleic acid section in the genome of a cell in order to allow a homologous recombination, and

(v) optionally a sequence encoding a negative selection marker.

25. A vector, comprising

(i) at least one sequence selected from the group consisting of a heterologous expression control sequence and an amplification gene each of which upon expression is capable of changing the expression of the nucleic acid sequence which is present endogenously in the cell,

(ii) a sequence encoding a positive selection marker,

- (iii) at least two recombinase target sequences flanking the sequences of (i) and (ii), and
- (iv) optionally a sequence encoding a negative selection marker.

28. A process for changing the expression of a nucleic acid sequence which is present endogenously in a eukaryotic cell, the method comprising

- (a) transfecting the cell with a vector comprising
  - (i) at least one nucleic acid sequence which binds an activator protein,
  - (ii) a sequence encoding a positive selection marker, and
  - (iii) DNA sequences which flank the sequences of (i) and (ii) and are homologous to a nucleic acid section in the genome of the cell in order to allow a homologous recombination,
- (b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place,
- (c) isolating the cell obtained according to step (b), and
- (d) expressing the sequence of (i) under conditions under which the activator protein is bound thereby changing the expression of the nucleic acid sequence which is present endogenously in the cell.

32. A vector suitable for homologous recombination, comprising the following sequences

- (i) at least one nucleic acid sequence which binds an activator protein,
- (ii) a sequence encoding a positive selection marker, and
- (iii) DNA sequences which flank the sequences of (i) and (ii) and are homologous to a nucleic acid section in the genome of a cell in order to allow a homologous recombination.

35. A process for testing the influence of non-coding nucleic acid sequences from the region of a target gene present endogenously in a eukaryotic cell on its expression, the process comprising

- (a) transfecting the cell with a vector comprising
  - (i) a heterologous expression control sequence which is active or can be activated in the cell and is operatively linked with a reporter gene, and
  - (ii) non-coding nucleic acid sequences on the 5'-side and/or the 3'-side from the region of the target gene,
- (b) culturing the cell under conditions under which the heterologous expression control sequence is active, and
- (c) measuring expression of the reporter gene.

36. A process for obtaining a DHFR-negative eukaryotic cell, the process comprising

- (a) transfecting a DHFR-positive cell with a first vector comprising
  - (i) at least one DHFR-negative target sequence for a site-specific recombinase;
  - (ii) DNA sequences which flank sequence (i) and are homologous to a DHFR nucleic acid sequence which is present endogenously in the cell in order to allow a homologous recombination,
  - (iii) optionally a sequence encoding a first positive selection marker, and
  - (iv) optionally a sequence encoding a negative selection marker,
- (b) culturing the transfected cell under conditions under which a homologous recombination of the vector takes place thereby incorporating the DHFR-negative target sequence into the DHFR-positive cell to create a DHFR-negative cell, and
- (c) isolating the cells obtained according to step (b) to obtain a DHFR-negative eukaryotic cell.

37. A process for obtaining a eukaryotic cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene, the process comprising

- (a) obtaining a DHFR-negative eukaryotic cell by the process as claimed in claim 36, (b) transfecting the cell of step (a) with a second vector comprising
- (i) a nucleic acid sequence coding for a DHFR,
  - (ii) a nucleic acid sequence to be amplified which codes for a protein in an expressible form,
  - (iii) optionally a sequence encoding a second positive selection marker, and
  - (iv) at least two recombinase target sequences flanking the sequences of (i), (ii) and (iii), if present,
- (c) culturing the transfected cell under conditions under which the sequences of (i), (ii) and (iii), if present, are integrated into the recombinase target sequence that is already present in the genome of the cell, and
- (d) isolating the cell obtained according to step (c) to obtain a eukaryotic cell containing a nucleic acid sequence to be amplified and a heterologous DHFR gene.

39. A vector, comprising

- (i) a nucleic acid sequence coding for a DHFR,
- (ii) a nucleic acid sequence to be amplified which codes for a protein in an expressible form,

(iii) optionally a sequence encoding a positive selection marker,  
and  
(iv) at least two recombinase target sequences flanking the  
sequences of (i), (ii) and (iii), if present.

40. A vector suitable for homologous recombination, comprising

(i) optionally a sequence encoding a positive selection marker,  
(ii) at least one recombinase target sequence which flanks the  
sequence of (i), if present,  
(iii) DNA sequences which flank the sequences of (i), if present,  
and (ii) and which are homologous to a DHFR nucleic acid sequence which is  
present endogenously in a cell in order to allow a homologous recombination,  
and  
(iv) optionally a sequence encoding a negative selection marker  
[gene] which is outside the homologous DNA sequences (iii).

#### **REMARKS**

Claims 20-43 are pending in this application. By this Amendment, Claims 20, 23-25, 28, 32, 35-37, 39, and 40 have been amended without prejudice to conform with the requirements of the Second Office Action.